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# PSILOCYBIN

The plant kingdom has provided man with an abundant source of medicinal and mind-altering substances. Cocaine from the coca plant, opium from the poppy, nicotine from tobacco, and mescaline from the peyote cactus are examples of these drugs. One such drug which has achieved prominence during the psychedelic era is psilocybin. Psilocybin occurs naturally in several species of mushrooms, notably Psilocybe mexicana.

## History

Teonanacatl ("food of the gods"), the sacred mushroom, has been used by Indian cultures of Mexico and Central America for centuries. The practice of incorporating a divine mushroom into a semi-religious ceremony dates back to 1500 B.C., based on stone artifacts believed to represent mushrooms. The first recorded use of hallucinogenic mushrooms occurred during the coronation feast of Montezuma in 1502. However, with the introduction of Christianity to the New World, the advocates of the mushroom rites were severely persecuted and the practice was driven underground.

In 1953, R. Gordon Wasson, a New York banker, and his wife, Valentina Pavlovna, rediscovered the ancient ritual of the Oaxacan Indians. The ritual is supervised by a curandero (priestess) and is conducted only when a specific problem arises. (This contrasts with the regular weekly use of peyote by the Native American Church of North America.) The Wassons described the taste of the mushrooms as acidic, similar to rancid grease, and unpleasant. Most important, the Wassons were able to secure specimens of the mushrooms being used. A French mycologist, Roger Heim, identified them as foliate mushrooms of the genus Psilocybe. He was also successful in cultivating this species in his laboratory from spores, thus providng sufficient material for chemists to isolate the active principal.

Subsequently, Albert Hofmann, the discoverer of lysergic acid diethylamide (LSD), and his colleagues at the Sandoz Laboratories in Basel, Switzerland, isolated two substances from Psilocybe mexicana Heim. Psilocybin (phosphorylated 4-hydroxydimethyltryptamine) was isolated as the major constituent; however psilocin (4-hydroxydimethyltryptamine) was also found in small amounts, but was equally active. These alkaloids have since been found present in numerous varieties of mushrooms of the genus Psilocybe as well as several other mushroom species. Interestingly, psilocybin is relatively unstable and upon ingestion is converted to psilocin by the enzyme, alkaline phosphatase. Therefore, it seems likely that psilocin is actually responsible for the drug effects accredited to psilocybin.

## Chemistry and Pharmacology

An hallucinogen, psilocybin exhibits a range of effects similar to those produced by LSD and mescaline, another organic alkaloid hallucinogen found in the mescal cactus. However, the potency of LSD is considerably greater than psilocybin, which in turn is more potent than mescaline. A dose of 225 micrograms per kilogram (mcg./kg.) of psilocybin would produce clinical effects comparable to 1 to 1.5 mcg./kg. of LSD or, in other words, 20 milligrams (mg.) of psilocybin would be approximately equivalent to the usual dose for an LSD "trip" (i.e., 100 mcg.). Tolerance to psilocybin has been demonstrated, although it does not occur as rapidly as tolerance to LSD. Individuals tolerant to psilocybin are also tolerant to a "challenging" dose of LSD. Similarly, individuals tolerant to LSD display cross-tolerance to psilocybin.

Toxicological studies with psilocybin are limited. Hofmann and his colleagues determined the LD-50 in mice (the "lethal dose" for 50 percent of the mice used in the experiment) as 280 mg./kg. There have been no indications of toxic effects produced by the drug in humans when used in controlled experiments. The Indians' use of the drug in its natural form provides little information as to its cumulative toxicity, since the mushrooms are not ingested in a chronic fashion. However, cases of poisoning from Psilocybe mushrooms have been reported in Oregon and Washington. Two adults and four children consumed what they thought to be edible mushrooms, later identified as Psilocyben baeocystes, which contained psilocybin and psilocin. All children developed a high fever (102° - 106°F.) and convulsions; one died.

## Patterns of Use

The use of psilocybin outside the realm of clinical research can be correlated with the use of other psychedelics, notably LSD. Initial use of these drugs occurred at several cosmopolitan universities in the mid 1960's and proliferated into the "youth ghettoes" of the large metropolitan centers of the East and West Coasts.

Two factors apparently led to the increased popularity of psilocybin: first, the limited availability of psilocybin as compared to LSD made it more attractive; and second, reports of LSD-induced genetic damage directed users toward mescaline and psilocybin. With the increased demand for these more "exotic" drugs, dealers began promoting LSD as "psilocybin" and "mescaline." Due to the illicit nature of psychedelic drug use, it is exceedingly difficult to accurately assess the contents of "street-produced" drug samples. However, recent chemical analyses of street "psilocybin" and "mescaline" have usually proven to be LSD or sometimes other drugs, such as PCP (phencyclidine).

LSD and psilocybin produce quite similar effects. However, because expectations play a significant role in the outcome of the psychedelic drug experience, users may report subjective differences between the LSD and the supposed psilocybin experience, although they took LSD both times. That is to say, the "folk knowledge" that circulates about the drug psilocybin may grossly affect the drug experience. Such "folk knowledge" includes: "psilocybin has a longer onset of action than does LSD;" "visual images frequently are in geometric or mosaic patterns;" and "colors are much more intense than those seen under LSD."

Although synthetic psilocybin is relatively rare, occasionally "organic" psilocybin appears as capsules containing powdered spores, or as entire mushrooms obtained from persons growing their own.

## Subjective Effects

The subjective experience produced by the hallucinogens, including psilocybin, is largely determined by the individual's set and setting. The set includes the following: the personality of the user; mood; expectations; and preparation (e.g., discussion and reading). The setting involves the environment in which the drug is taken, that is, the degree to which the immediate surroundings are comfortable. This may include such situational factors as music, intensity of light, and presence of friends. The set and setting greatly affect the outcome of the "trip."

In a clinical setting, Dr. Leo E. Hollister described the pattern of subjective effects in normal subjects given doses of 115 to 160 mcg./kg. orally as follows:

> First 30 minutes--Dizziness, light-headedness or giddiness; weakness, muscle aching and twitching, shivering; nausea, abdominal discomfort; anxiety, tension, restlessness; numbness of the tongue, lips or mouth; heaviness or lightness of the extremities;
>
> 30 to 60 minutes--Blurred vision, brighter colors, longer after-images, sharp definition of objects, visual patterns (eyes closed); increased acuity of hearing; yawning, tearing, facial flushing, sweating; dreamy state, loss of attention and concentration; slow thinking, feelings of unreality, depersonalization; incoordination, difficult and tremulous speech;
>
> 60 to 90 minutes--Increased visual effects (colored patterns and shapes, generally pleasing, sometimes frightening, most often with eyes closed, occasionally superimposed upon objects in field of vision); undulation of viewed surfaces; distance perception impaired; euphoria, general stimulation, ruminative state; slowed passage of time;
>
> 90 to 120 minutes--Continuation of many of the above effects in varying degrees, especially introspective state; increased bodily sensations and mental perceptions;
>
> 120 to 180 minutes--waning of previously described effects;
>
> 180 to 300 minutes--Nearly complete resolution of drug-induced effects.

Other effects reported, although not as frequently as those outlined above included: decreased salivation and appetite; transient sexual feelings and synesthesias (e.g., "seeing" sounds). Hollister also found that when comparable doses of psilocybin were administered by injection, the pattern of effects was similar; however, onset of effects occurred after only five minutes and the syndrome produced was more intense and of longer duration.

For comparison with the clinical experience, the following is an excerpt of Wasson's experience with the psilocybin mushroom:

> The sacred mushrooms of Mexico seize hold of you with irresistible power. They lead to a temporary schizophrenia, or pseudoschizophrenia, in which your body lies, heavy as lead, on the petate, or mat, and you take notes and compare experiences with your neighbor, while your soul flies off to the ends of the world and, indeed, to other planes of existence. The mushrooms take effect differently with different persons. For

> example, some seem to experience only a divine euphoria, which may translate itself into uncontrollable laughter. In my case I experienced hallucinations. What I was seeing was more clearly seen than anything I had seen before. At last I was seeing with the eye of the soul, not through the coarse lenses of my natural eyes. Moreover, what I was seeing was impregnated with weighty meaning: I was awe-struck.

## Animal Behavior

Sandoz Laboratories reported that no behavioral effects were apparent in mice following subcutaneous doses of psilocybin below 10 mg./kg. or in rabbits receiving 1 mg./kg. intravenously. Higher doses were found to produce a reduction in activity. Similarly, a slight quieting effect was noted following ingestion of 10 mg./kg. by monkeys. Intravenous injection of 3.5 mg./kg. of psilocybin in rabbits was found to produce marked behavioral effects after 20 to 30 minutes (Steiner and Sulman). These included increased water intake, irritability, anxiety, chewing, licking, spontaneous motor activity and vocalization.

Mice given psilocybin displayed a shorter reaction time on the hot plate test, according to the Sandoz report. Also, no alteration of the convulsive threshold in mice to electric or metrazole shock was elicited by psilocybin.

## Psychological Effects

The first American studies giving psilocybin to humans were conducted by Rinkel et al. Four male volunteers received 5 to 10 mg. of psilocybin sublingually (under the tongue). Visual perception and thought process were minimally altered. No hallucinations were reported. All subjects experienced changes in mood, characterized by euphoria and dysphoria. Two of the subjects were more relaxed and sleepy, while the other two were more active. Speech was either slow or rapid and at times slurred. Concentration was disturbed in all subjects; three subjects experienced time perception alteration, and one subject experienced feelings of depersonalization.

Hollister (1961) found that performance on psychometric tests (Number Facility Test and Flexibility of Closure) was decreased for one to two hours following administration of psilocybin. However, it was suggested the poor performance might be related to decreased motivation. That is, an individual participating in hallucinogenic drug research is often not interested in performing the experimental tasks presented by the scientist, but would rather concentrate on the subjective experience produced by the drug. Since the drug experience is highly subjective, the laboratory setting affects the experience also.

Keeler (1963) examined changes in critical flicker fusion (CFF) in two subjects receiving 0.05 mg./kg. psilocybin and in five subjects receiving 0.2 mg./kg. A correspondence between alterations in CFF and subjective response (as measured by a 76-question check list developed by H. Abramson) was "fairly but not precisely consistent." In one of the subjects receiving a low dose, CFF was elevated despite the absence of a definite subjective response, Keeler suggests that subjective drug effect and CFF may reflect similar basic processes.

In a double-blind study, Keeler (1965) demonstrated that psilocybin (0.2 mg./kg. oral) significantly prolonged after-image perception as compared to controls. Also the changes observed in the objective measure of after-image perception were found to be highly correlated with reports of altered visual experience.

Fischer and Rockey administered 10 to 12 mg. of psilocybin orally to seventeen volunteer college students who, at the peak of the drug effect, were requested to read a set of printed texts in which presentation of the letters was scaled down in three steps to a "text" in which 74% of the individually printed characters were invisible. As compared to controls, four subjects were able to correctly read up to 42% of the text in which the letters had 74% of their uppermost height deleted. The authors interpreted this as evidence of increased ability to form closure, recall of past experience or increased expectation. They felt that closure-making (i.e., the transformation of information to meaning) is basic to artistic creation.

In a recent study of the effects of psilocybin (10 mg.) on 22 staff members of the Mayo Clinic, Rynearson et al. documented the following effects: seventeen subjects reported distortions of vision, hearing and touch; generalized numbness and sensations of lightness or heaviness of the limbs were experienced by 19 subjects; twenty of the subjects exhibited anxiety as an early symptom; euphoria was prevalent with 18 subjects experiencing uncontrolled laughter; extreme fatigue and weariness manifested itself in all subjects following the drug experience and persisted from 3 to 36 hours; no lasting psychopathological changes were evident from data collected from the Minnesota Multiphasic Personality Inventory (MMPI) and Thematic Apperception Test (TAT) administered from 2 to 14 days following the experiment.

The most marked psychological effects produced by psilocybin and other psychedelic drugs are the dramatic sensory changes. These perceptual alterations, usually visual, are recognized by the subject under the influence of a psychedelic drug as manifestations of the drug experience, thereby having no basis in "reality." These sensory changes, therefore, are not true hallucinations as experienced by schizophrenics, but may be more appropriately termed illusions.

## Physiological Effects

The physiological effects produced by psilocybin are not unlike those seen with LSD. These effects are usually minimal and tend to be mediated by the autonomic nervous system. Common physiological changes include: pupillary dilation; increased deep tendon reflexes; slight increases in pulse, blood pressure and body temperature.

Hollister (1961) reported that urinary excretion of inorganic phosphorus and total circulating eosinophils were significantly reduced. Hollister also found increased free fatty acid (FFA) levels indicative of stress in fasting subjects given psilocybin, mescaline or LSD. It is difficult to discern whether these biochemical changes are effective monitors of the drug's mode of action, or if these alterations are indicative of anxiety produced by psilocybin.

## Treatment

The main dangers associated with psilocybin, as well as the other hallucinogens and marihuana, are primarily psychological in nature. These may be evidenced as intense anxiety or panic states ("bad trips"), depressive or paranoid reactions, mood changes, disorientation and an inability to distinguish between reality and fantasy. Some prolonged psychotic reactions to psychedelic drugs have been reported, particularly with persons already psychologically disturbed.

The "talk-down" technique has been established as the preferred method for handling "bad trips." This technique involves non-moralizing, comforting, personal support from an experienced individual. This is aided by limiting external stimulation such as intense light or loud sounds and having the person lie down and relax.

Although use of tranquilizers (e.g., phenothiazines) is widespread, these drugs should only be employed to "abort" the psychedelic drug experience if "talking down" has failed. Several problems may arise from the use of tranquilizers or other sedatives including: possible undesirable interactions with unknown street drugs or contaminated drugs; creation of a more confusing picture, which is harder for the physician to diagnose and treat; a paradoxical response potentiating the drug effects; and increasing the possibility of subsequent flashbacks (recurrences).

## Legal Aspects

Psilocybin and psilocin are considered controlled dangerous substances under the Comprehensive Drug Abuse Prevention and Control Act of 1970. Illegal possession of psilocybin or psilocin (in synthetic or organic form) can result in a sentence to a term of imprisonment of not more than one year, a fine of not more than $5,000, or both. Conviction of illicit manufacture or sale can result in a sentence to a term of imprisonment of not more than 5 years, a fine of not more than $15,000, or both. Subsequent convictions would result in increased penalties.

## Comments

The psychedelic drugs, including psilocybin, have for decades been the subject of extensive scientific research. These drugs have gained further attention by the non-scientific community as substances which "expand consciousness" and which have opened areas of self-investigation previously unrecognized.

> I don't know what psilocybin does for other people, but for me it has been profoundly healing and illuminating.
>
> Alan Watts, D.D.

A determination must be made by the user as to whether the benefits derived from the drug are outweighed by potential detrimental effects.

> The use of psychotomimetic drugs as therapeutic agents in an out-patient setting may prove potentially hazardous. Acute states of excitement, depression with suicidal ideation and impairment of judgment may occur with these drugs, even in the most carefully supervised in-patient setting. With out-patients, the danger of self-administration and inadequate supervision could compound such occurrences.
>
> Sidney Malitz, M.D. et al.

Perhaps, knowledge of the drug's effects and the concomitant non-pharmacological factors may assist in making this assessment.

> LSD and related drugs induce bizarre and often threatening experiences which may be used productively by individuals with well-integrated personalities. On the other hand, they can severely shake an adolescent's already tenuous conception of self, further disrupting a crucial period of psycho-social development.
>
> Samuel Irwin, Ph.D.

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